ABSTRACT

This study will evaluate the safety and efficacy of *in vivo* gene transfer of the herpes simplex thymidine kinase (HSV-Tk1) gene using PA317/G1Tk1SvNa.7 vector producer cells (VPCs) in patients with recurrent malignant glioma. Insertion of the HSV-Tk1 gene confers sensitivity to the anti-herpes drug ganciclovir. It has been demonstrated that the direct injection of the HSV-Tk vector producer cells into growing tumors in animals can result in their complete destruction with ganciclovir therapy. In addition, complete tumor ablation has been demonstrated in animal tumor models with HSV-Tk1 and ganciclovir. This selective destruction of growing tumors *in situ* is thought to result from the transfer of the HSV-Tk1 gene into the tumor cells and the production of toxic ganciclovir metabolites which result from the interaction of HSV-Tk1 and ganciclovir. This procedure can result in the cure of some experimental animals with limited systemic toxicity due to selective gene transfer into tumors.

This clinical trial will focus on maximizing the relative number of vector producer cells to the tumor mass by stereotactically injecting VPCs in to the tumor mass. Adults with recurrent malignant glioma which is accessible to stereotactic injection will be evaluated for the extent and location(s) of their disease before being entered into the study. Fifteen days after stereotactic injection of the tumor mass, ganciclovir will be administered at 5 mg/kg IV b.i.d. for 14 days. Upon completion of the treatment with HSV-Tk1 vector producer cells and ganciclovir, patients will be followed monthly for the first three months, then every **two** months for the next **twenty-two** months, and annually for life thereafter.